Figure 1(A)

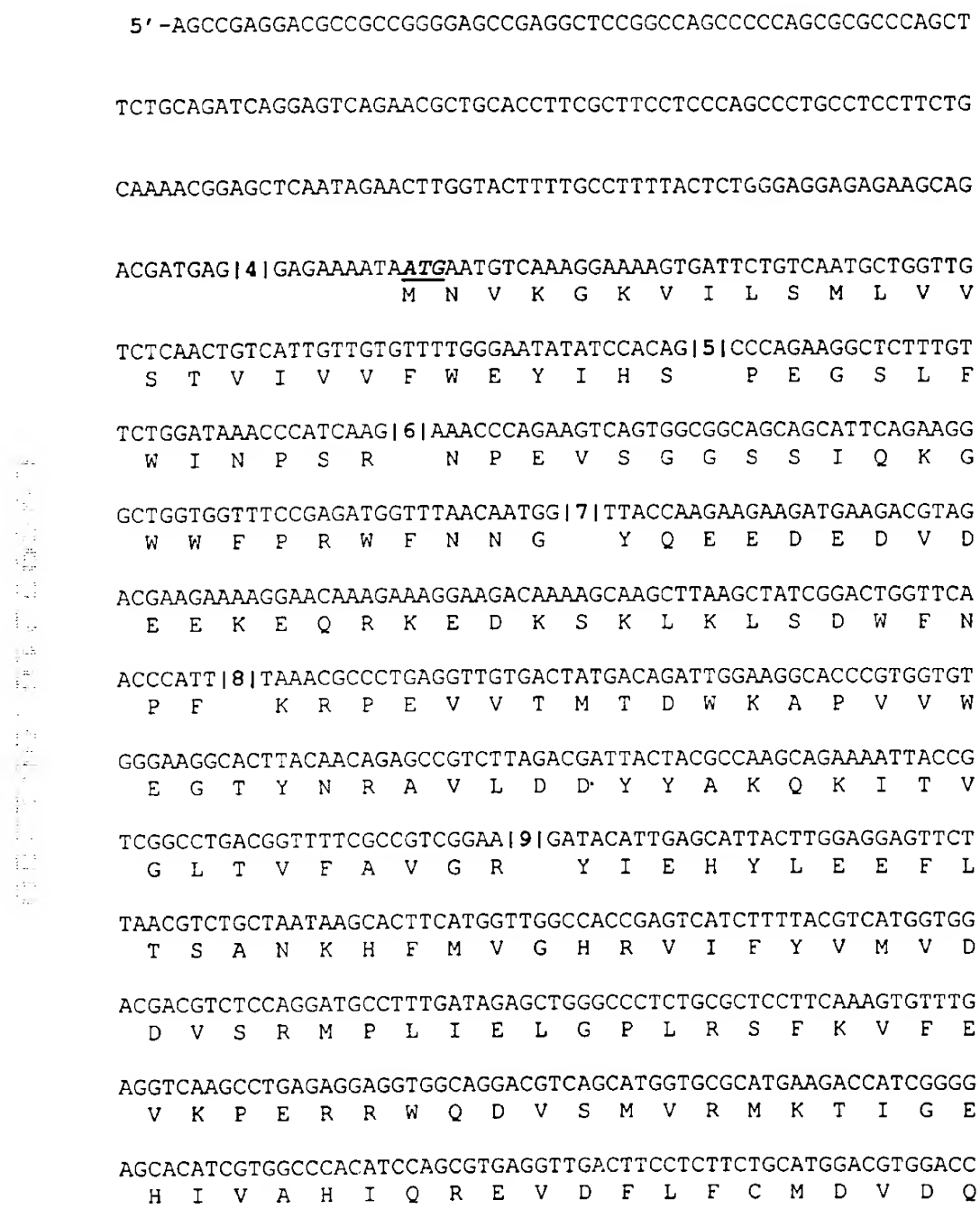


Figure 1(B)

AGGTCTTCCAAGACGAGTTCGGGGTGGAGACCCTGGGTGAGTCGGTGGCCCAGCTACAGG
V F Q D E F G V E T L G E S V A Q L Q A

CCTGGTGGTACAAGGCAGATCCCGATGAGTTTACCTACGAGAGGCGCAAGGAGTCTGCAG
W W Y K A D P D E F T Y E R R K E S A A

CATACATTCCCTTCGGCGAAGGGGATTTTTATTACCACGCAGCCATTTTTGGGGGAACAC
Y I P F G E G D F Y Y H A A I F G G T P

CCACTCAGGTCCTTAACATCACCCAGGAATGCTTCAAAGGAATCCTCAAGGACAAGAAAA
T Q V L N I T Q E C F K G I L K D K K N

ATGACATAGAAGCCCAATGGCATGATGAGAGCCATCTAAACAAGTATTTCCTTCTCAACA
D I E A Q W H D E S H L N K Y F L L N K

AACCCACTAAAATCTTATCCCCGGAATACTGCTGGGATTATCATATAGGCCTACCTGCGG
P T K I L S P E Y C W D Y H I G L P A D

ATATTAAGCTTGTCAAGATGTCTTGGCAGACAAAAGAGTATAATGTGGTTAGAAATAACG
I K L V K M S W Q T K E Y N V V R N N V

TC***TGA***AGCCGAGGACGCCGCCGGGGAGCCGAGGCTCCGGCCAGCCCCCAGCGCGCCCAGC

TTCTGCAGATCAGGAGTCAGAACGCTGCACCTTCGCTTCCTCCCAGCCCTGCCTCCTTCT

GCAAAACGGAGCTCAATAGAACTTGGTACTTTTGCCTTTTACTCTGGGAGGAGAGAAGCA

GACGATGAGGAGAAAATA

Figure 2(A)

```
sheep       ------------------------------------------------------------
bovine      CCGGGGGCCGGGCCGAGCTGGGAGCGTCGAGCCCGCTGCCCAGCGCCCGCCGGCTCCCTC

sheep       ------------------------------------------------------------
bovine
            GCGCCCCTGCCCGCCGCCCCGGAGGAGCGCCCGGCGGCCGGCCGACGGGAGCGCAGCGGC

sheep       ------------------------------------------------------------
bovine      ACACCCCGCCCCGGCACGCCCGCGGGGCTCGGGAGGAGGCAGCGCGCCGACTGTTCCGGC

sheep       AGCCGAGGACGCCGCCGGGGAGCCGAGGCTCCGGCCAGCCCCCAGCGCGCCCAGCTTCTG
bovine      AGCCGAGGACGCCGCCGGGGAGCCGAGGCGCCGGCCAGCCCCCAGCGCGCCCAGCTTCTG
            ****************************** ******************************

sheep       CAGATCAGG----------------------------------------------------
bovine      CGGATCAGGGAAACCACGTGTCCTCAAGTGGCCAGCCAGCTGTCCCCAAGAGGAACTTGC
            * *******

sheep       ---------------------------------------------AGTCAGAACGCTGCAC
bovine      CTGGCATTTGCACGGAAAGACGAGACACTTCACAAAATCAACGGAGTCAGAAGGCTGCAC
                                                        ******** *******

sheep       CTTCGCTTCCTCCCAGCCCTGCCTCCTTCTGCAAAACGGAGCTCAATAGAACTTGGTACT
bovine      CTTCGCTTCCTCCCAGCCCTGCCTCCTTCTGCAGAACGGAGCTCAGTAGAACTTGGTACT
            ********************************** ********** **************
                                                        ⇓
sheep       TTTGCCTTTTACTCTGGGAGGAGAGAAGCAGACGATGAGGAGAAAATAATGAATGTCAAA
bovine      TTTGCCTTTTACTCTAGGAGGAGAGAAGCAGACGATGAGGAGAAAATAATGAATGTCAAA
            *************** ********************************************

sheep       GGAAAAGTGATTCTGTCAATGCTGGTTGTCTCAACTGTCATTGTTGTGTTTTGGGAATAT
bovine      GGAAAAGTGATTCTGTCAATGCTGGTTGTCTCAACTGTCATTGTTGTGTTTTGGGAATAT
            ************************************************************

sheep       ATCCACAGCCCAGAAGGCTCTTTGTTCTGGATAAACCCATCAAGAAACCCAGAAGTCAGT
bovine      ATCCACAGCCCAGAAGGCTCTTTGTTCTGGATAAACCCATCAAGAAACCCAGAAGT---T
            ************************************************************   *

sheep       GGCGGCAGCAGCATTCAGAAGGGCTGGTGGTTTCCGAGATGGTTTAACAATGGTTACCAA
bovine      GGTGGCAGCAGCATTCAGAAGGGCTGGTGGCTTCCGAGATGGTTTAACAATGGTTACCAT
            ** ************************** ****************************
```

Figure 2(B)

```
sheep     GAAGAAGATGAAGACGTAGACGAAGAAAAGGAACAAAGAAAGGAAGACAAAAGCAAGCTT
bovine    GAAGAAGATGGAGACATAAACGAAGAAAAGGAACAAAGAAACGAAGACGAAAGCAAGCTT
          ********** **** ** ********************** ****** **********

sheep     AAGCTATCGGACTGGTTCAACCCATTTAAACGCCCTGAGGTTGTGACTATGACAGATTGG
bovine    AAGCTATCGGACTGGTTCAACCCATTTAAACGCCCCGAGGTTGTGACCATGACGAAGTGG
          ************************************ ********** *****  * ***

sheep     AAGGCACCCGTGGTGTGGGAAGGCACTTACAACAGAGCCGTCTTAGACGATTACTACGCC
bovine    AAGGCTCCAGTGGTGTGGGAAGGCACTTACAACAGAGCCGTCTTAGACAATTATTATGCC
          ***** ** ****************************************** **** ** ***

sheep     AAGCAGAAAATTACCGTCGGCCTGACGGTTTTCGCCGTCGGAAGATACATTGAGCATTAC
bovine    AAGCAGAAAATTACCGTCGGCCTGACGGTTTTCGCCGTCGGAAGATACATTGAGCATTAC
          ************************************************************

sheep     TTGGAGGAGTTCTTAACGTCTGCTAATAAGCACTTCATGGTTGGCCACCGAGTCATCTTT
bovine    TTGGAGGAGTTCTTAACGTCTGCTAATAAGCACTTCATGGTGGGCCACCCAGTCATCTTT
          ******************************************* ******* **********

sheep     TACGTCATGGTGGACGACGTCTCCAGGATGCCTTTGATAGAGCTGGGCCCTCTGCGCTCC
bovine    TATATCATGGTAGATGATGTCTCCAGGATGCCTTTGATAGAGTTGGGTCCTCTGCGCTCC
          **  ******* ** ** ************************ **** ************

sheep     TTCAAAGTGTTTGAGGTCAAGCCTGAGAGGAGGTGGCAGGACGTCAGCATGGTGCGCATG
bovine    TTCAAAGTGTTTAAGATCAAGCCTGAGAAGAGGTGGCAGGACATCAGCATGATGCGCATG
          ************ ** ************ ************* ******** ********

sheep     AAGACCATCGGGGAGCACATCGTGGCCCACATCCAGCGTGAGGTTGACTTCCTCTTCTGC
bovine    AAGACTATCGGGGAGCACATTGTGGCCCACATCCAGCATGAGGTTGACTTCCTTTTCTGC
          ***** ************** ***************** *************** ******

sheep     ATGGACGTGGACCAGGTCTTCCAAGACGAGTTCGGGGTGGAGACCCTGGGTGAGTCGGTG
bovine    ATGGATGTGGACCAGGTCTTCCAAGACAAGTTTGGGGTGGAGACCCTGGGCGAGTCGGTG
          ***** ********************** **** ***************** *********

sheep     GCCCAGCTACAGGCCTGGTGGTACAAGGCAGATCCCGATGAGTTTACCTACGAGAGGCGC
bovine    GCCCAGCTACAAGCCTGGTGGTACAAGGCAGATCCCAATGACTTCACCTACGAGAGGCGG
          *********** ************************ **** ** **************

sheep     AAGGAGTCTGCAGCATACATTCCCTTCGGCGAAGGGGATTTTTATTACCACGCAGCCATT
bovine    AAGGAGTCTGCAGCATACATTCCCTTCGGCGAAGGGGATTTTTATTACCATGCAGCCATT
          ************************************************* *********
```

Figure 2(C)

```
sheep       TTTGGGGGAACACCCACTCAGGTCCTTAACATCACCCAGGAATGCTTCAAAGGAATCCTC
bovine      TTTGGGGGAACACCCACTCAGGTCCTTAACATCACCCAGGAATGCTTCAAAGGAATCCTC
            ************************************************************

sheep       AAGGACAAGAAAAATGACATAGAAGCCCAATGGCATGATGAGAGCCATCTAAACAAGTAT
bovine      AAGGACAAGAAAAATGACATAGAAGCCCAATGGCATGATGAAAGCCATCTAAACAAGTAT
            ****************************************** ******************

sheep       TTCCTTCTCAACAAACCCACTAAAATCTTATCCCCGGAATACTGCTGGGATTATCATATA
bovine      TTCCTTCTCAACAAACCTACTAAAATCTTATCCCCGGAATACTGCTGGGATTATCACATA
            ***************** ************************************** ***

sheep       GGCCTACCTGCGGATATTAAGCTTGTCAAGATGTCTTGGCAGACAAAAGAGTATAATGTG
bovine      GGCCTACCTGCGGATATTAAGCTTGTCAAGATGTCTTGGCAGACAAAAGAGTATAATGTG
            ************************************************************

sheep       GTTAGAAATAACGTCTGA----------------------------------------
bovine      GTTAGAAATAATGTCTGACTTTGTGCCAGTACATTTCTGAATTTGAGAGAGTATTATTCT
            *********** ******
```

Figure 3

```
          1                                                50
bovine    MNVKGKVILS MLVVSTVIVV FWEYIHSPEG SLFWINPSRN PEV.GGSSIQ
sheep     MNVKGKVILS MLVVSTVIVV FWEYIHSPEG SLFWINPSRN PEVSGGSSIQ
          ********** ********** ********** ********** *** ******

          51                                              100
bovine    KGWWLPRWFN NGYHEEDGDI NEEKEQRNED ESKLKLSDWF NPFKRPEVVT
sheep     KGWWFPRWFN NGYQEEDEDV DEEKEQRKED KSKLKLSDWF NPFKRPEVVT
          **** ***** *** *** *   ****** **  ********* **********

          101                                             150
bovine    MTKWKAPVVW EGTYNRAVLD NYYAKQKITV GLTVFAVGRY IEHYLEEFLT
sheep     MTDWKAPVVW EGTYNRAVLD DYYAKQKITV GLTVFAVGRY IEHYLEEFLT
          ** ******* **********  ********* ********** **********

          151                                             200
bovine    SANKHFMVGH PVIFYIMVDD VSRMPLIELG PLRSFKVFKI KPEKRWQDIS
sheep     SANKHFMVGH RVIFYVMVDD VSRMPLIELG PLRSFKVFEV KPERRWQDVS
          **********  **** **** ********** ********   *** **** *

          201                                             250
bovine    MMRMKTIGEH IVAHIQHEVD FLFCMDVDQV FQDKFGVETL GESVAQLQAW
sheep     MVRMKTIGEH IVAHIQREVD FLFCMDVDQV FQDEFGVETL GESVAQLQAW
          ******** ****** *** ********** *** ****** **********

          251                                             300
bovine    WYKADPNDFT YERRKESAAY IPFGEGDFYY HAAIFGGTPT QVLNITQECF
sheep     WYKADPDEFT YERRKESAAY IPFGEGDFYY HAAIFGGTPT QVLNITQECF
          ******  ** ********** ********** ********** **********

          301                                             350
bovine    KGILKDKKND IEAQWHDESH LNKYFLLNKP TKILSPEYCW DYHIGLPADI
sheep     KGILKDKKND IEAQWHDESH LNKYFLLNKP TKILSPEYCW DYHIGLPADI
          ********** ********** ********** ********** **********

          351                 370
bovine    KLVKMSWQTK EYNVVRNNV*
sheep     KLVKMSWQTK EYNVVRNNV*
          ********** *********
```

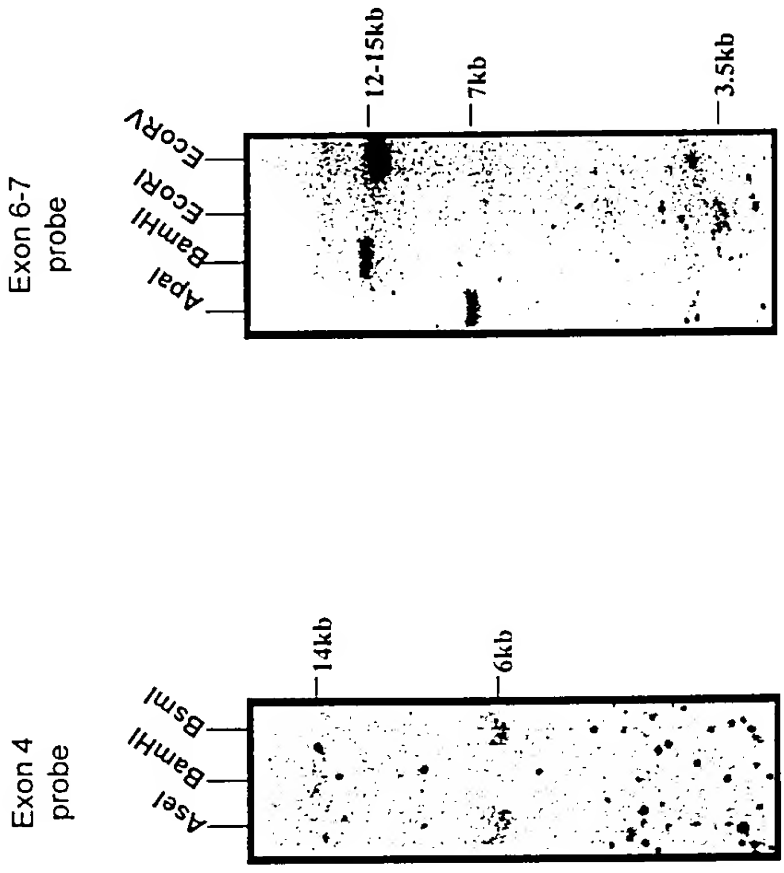


Figure 4

Figure 5

α(1,3)-GT GapDH

Figure 6

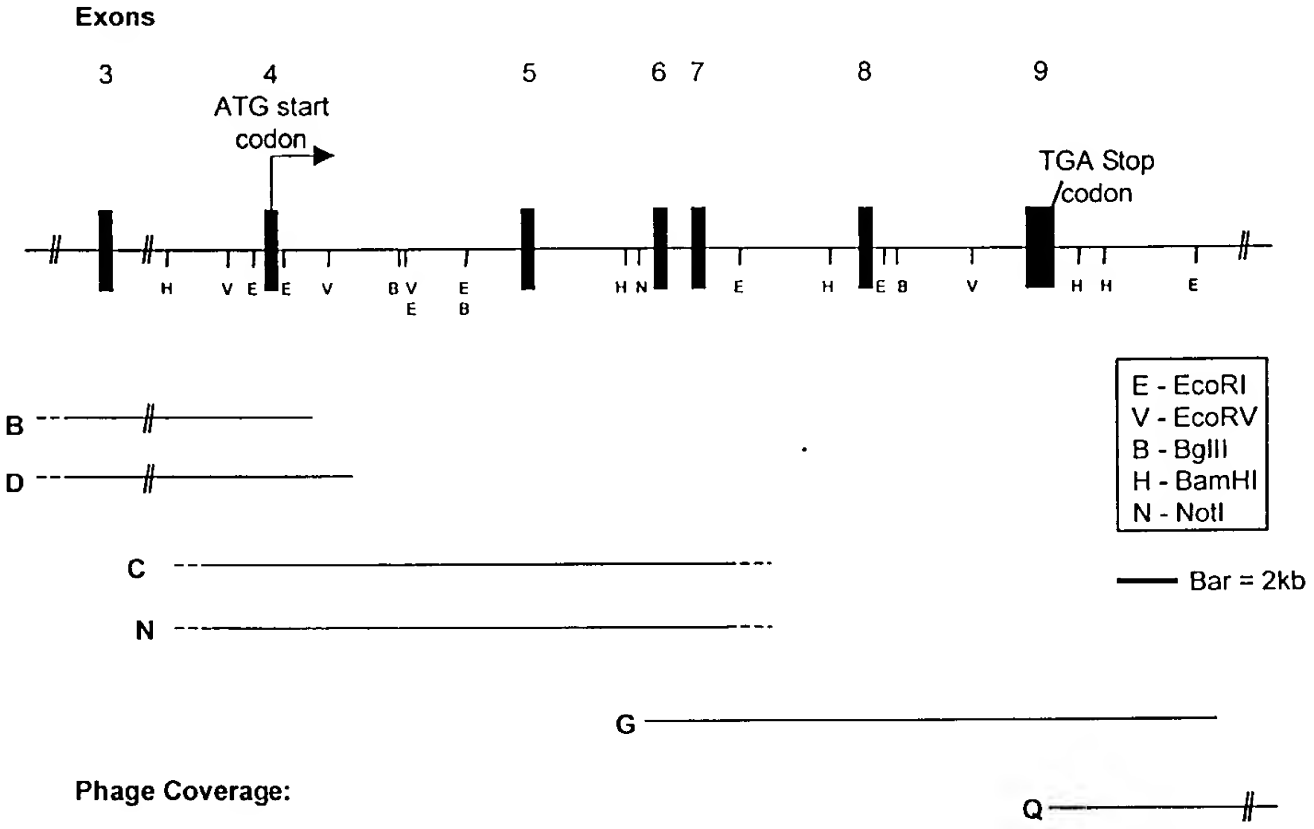


Figure 7

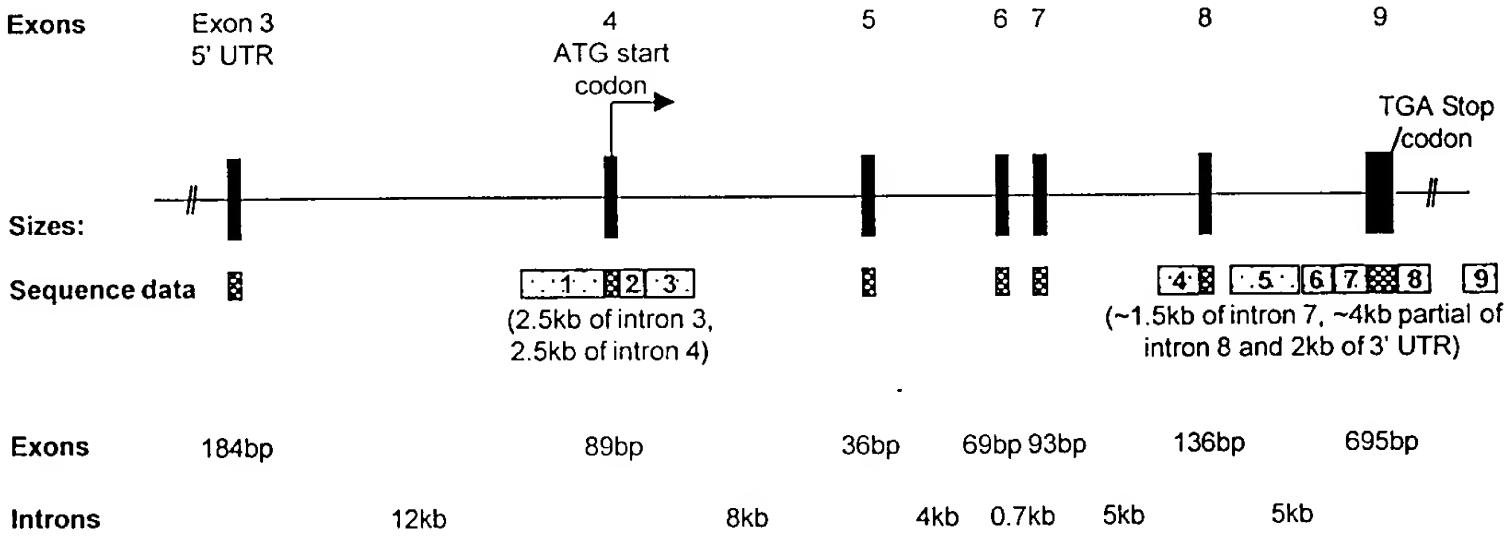

Exons
Exon 3
5' UTR
4
ATG start
codon
5
6 7
8
9
TGA Stop
codon
Sizes:
Sequence data
1 2 3
(2.5kb of intron 3,
2.5kb of intron 4)
4 5 6 7 8 9
(~1.5kb of intron 7, ~4kb partial of
intron 8 and 2kb of 3' UTR)
Exons
184bp
89bp
36bp
69bp
93bp
136bp
695bp
Introns
12kb
8kb
4kb
0.7kb
5kb
5kb

Figure 8

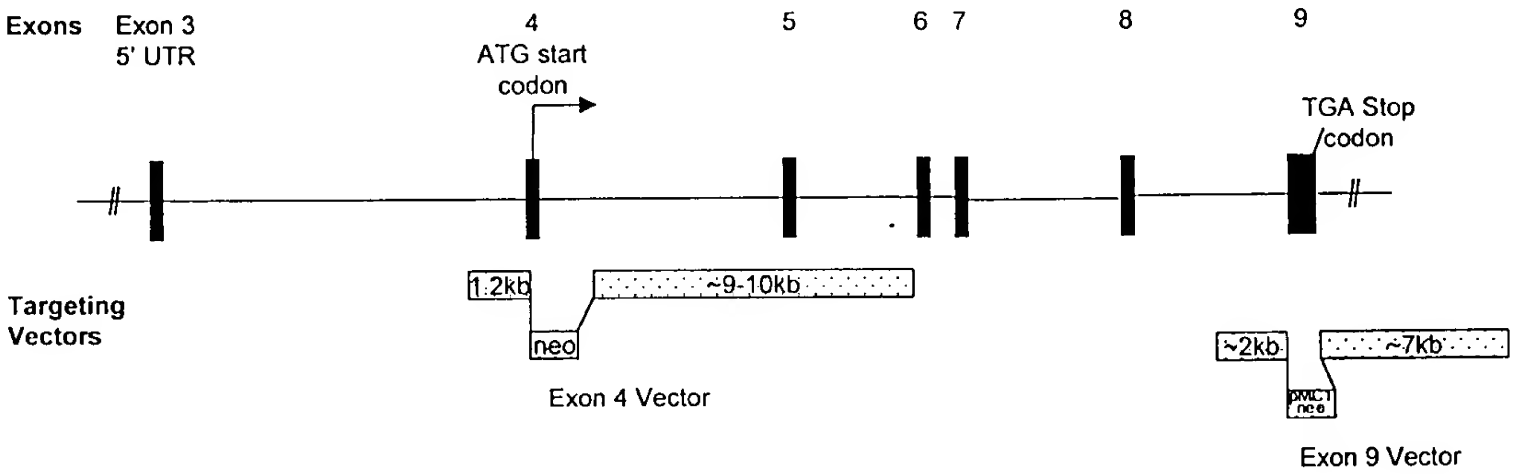

Exons
Exon 3
5' UTR
4
ATG start
codon
5
6
7
8
9
TGA Stop
codon
Targeting
Vectors
1.2kb
neo
~9-10kb
Exon 4 Vector
~2kb
pMC1
neo
~7kb
Exon 9 Vector

Figure 9

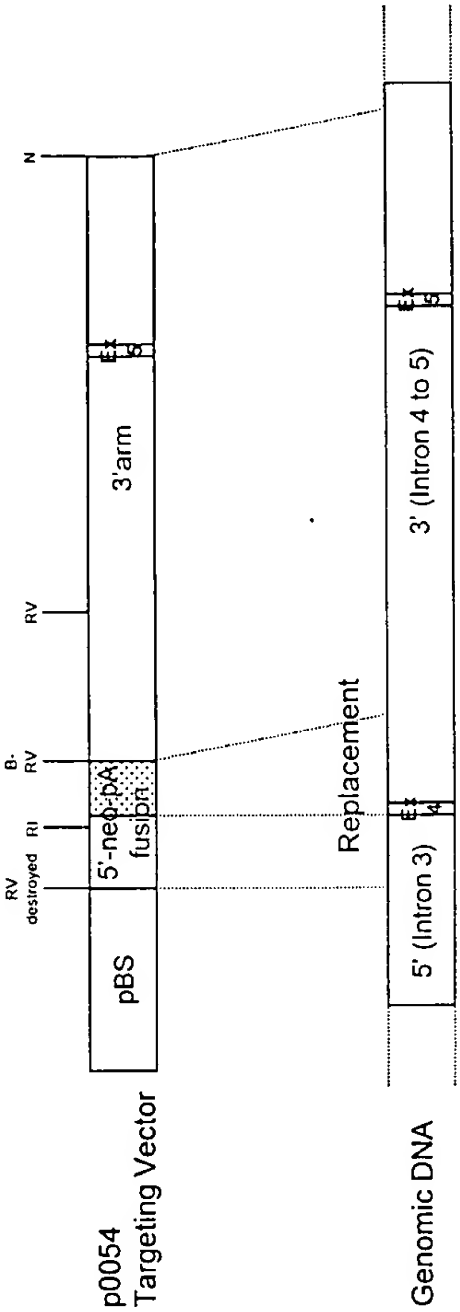
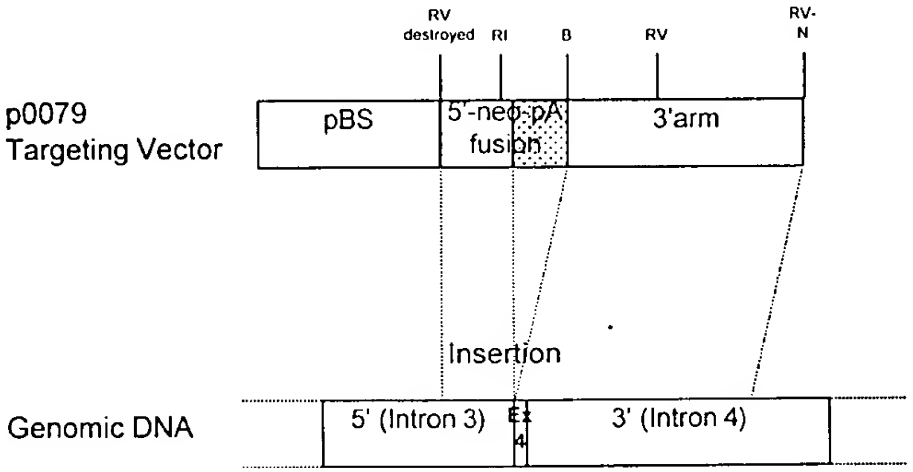


Figure 10



B - BamHI
N - NotI
RI - EcoRI
RV - EcoRV

= 1kb

Figure 11

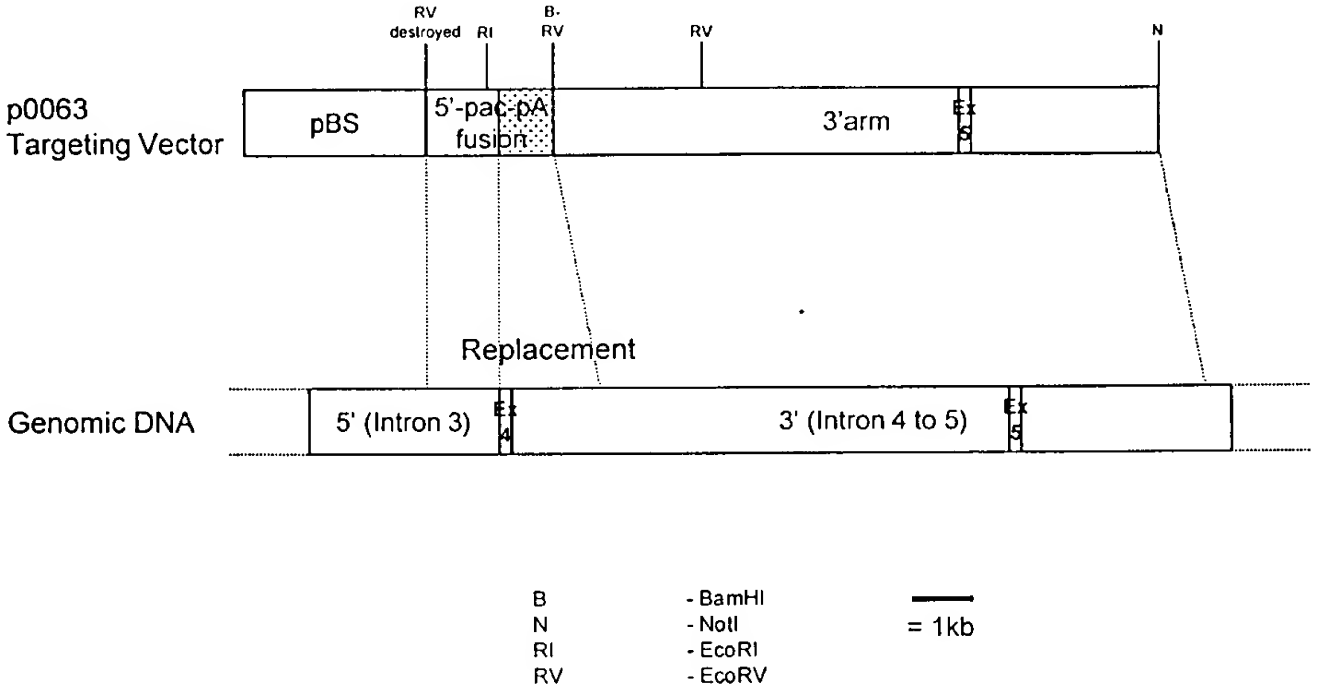


Figure 12

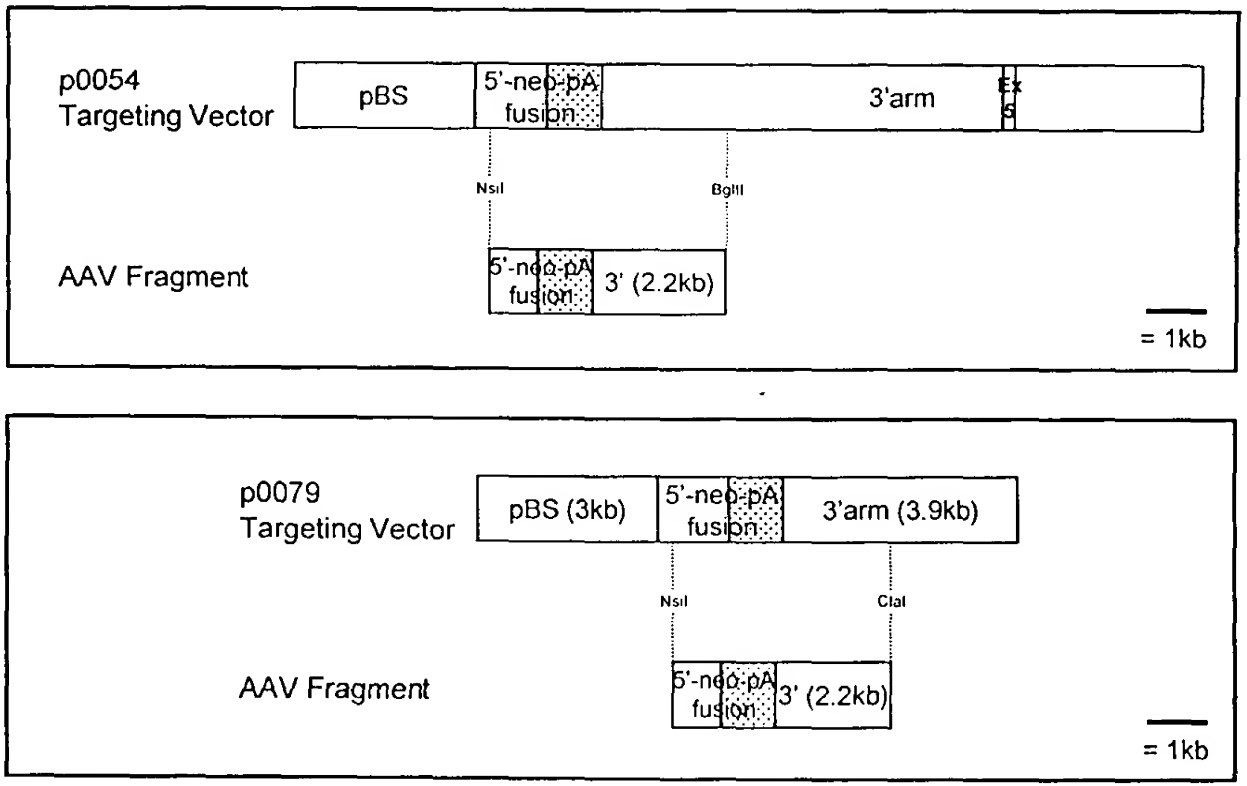
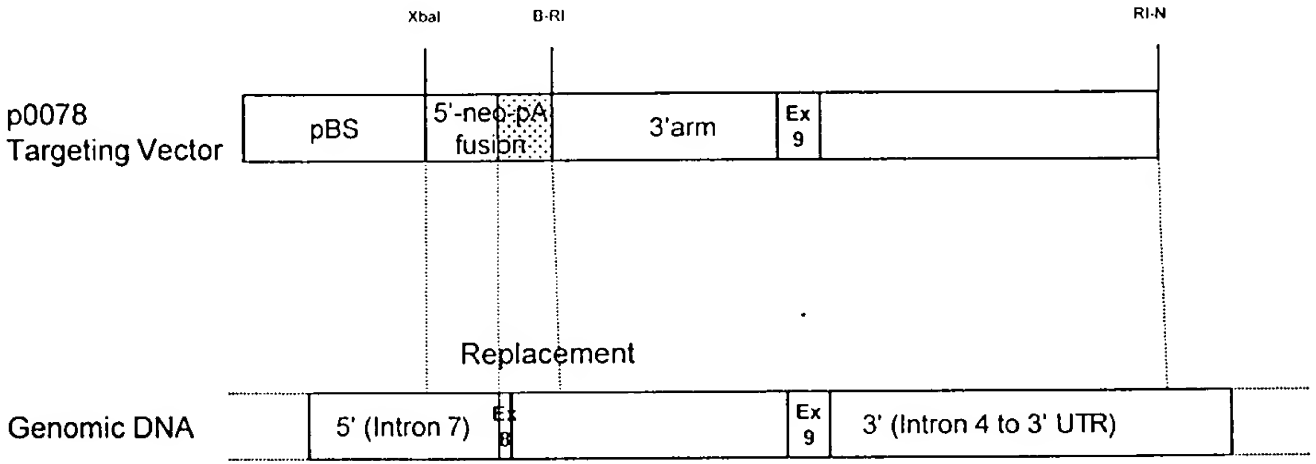


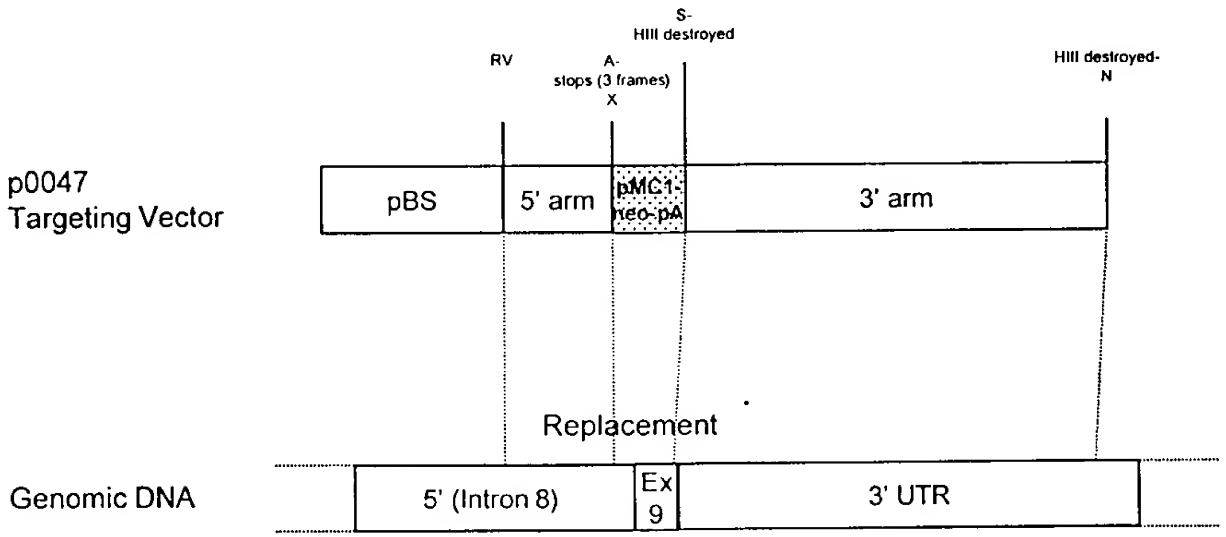
Figure 13



B - BamHI
N - NotI
RI - EcoRI
RV - EcoRV

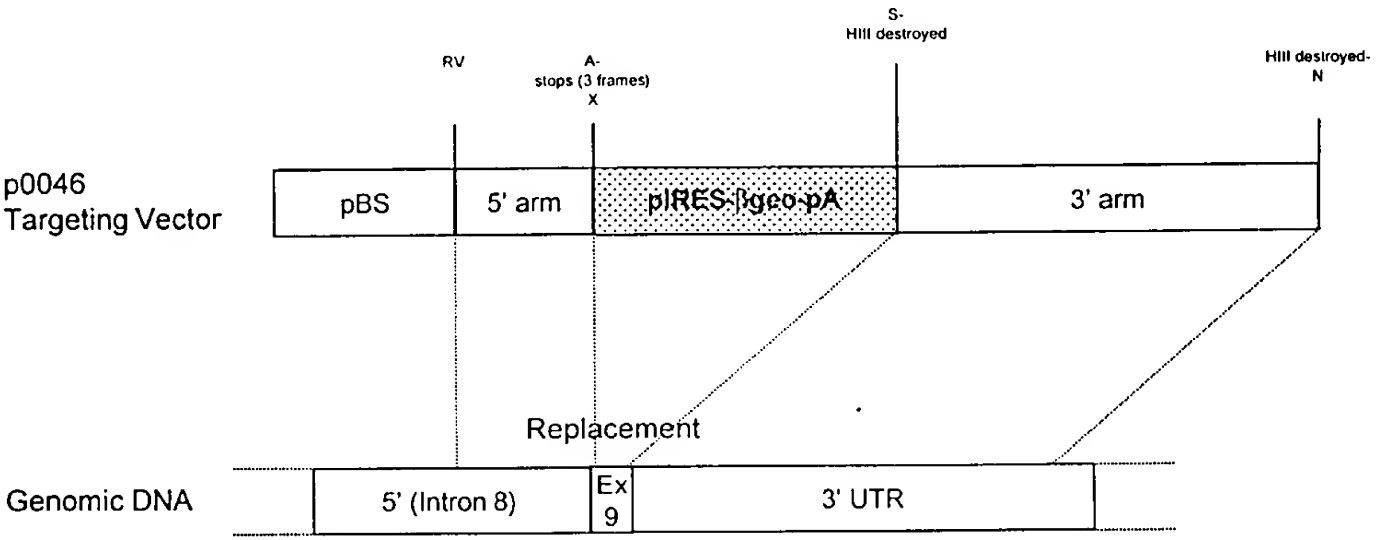
= 1kb

Figure 14



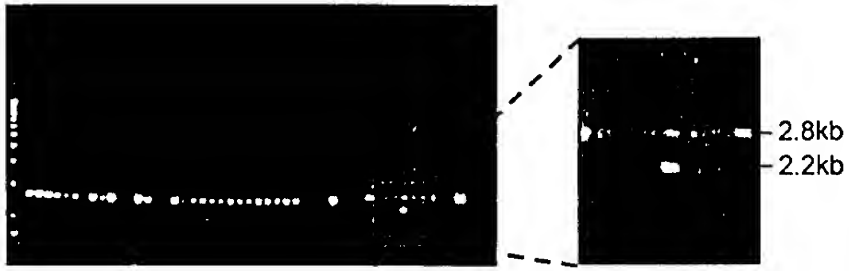
A	- ApaI	
H	- HinDIII	= 1kb
N	- NotI	
RV	- EcoRV	
S	- SalI	
X	- XhoI	

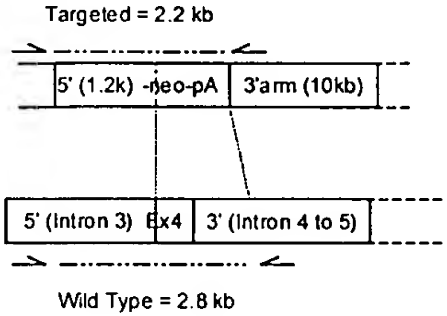
Figure 15



A	- ApaI	▬
H	- HinDIII	= 1cm
N	- NotI	
RV	- EcoRV	
S	- SalI	
X	- XhoI	

Figure 16


2.8kb
2.2kb


Targeted = 2.2 kb
5' (1.2k) -neo-pA
3'arm (10kb)
5' (Intron 3)
Ex4
3' (Intron 4 to 5)
Wild Type = 2.8 kb


1.5kb

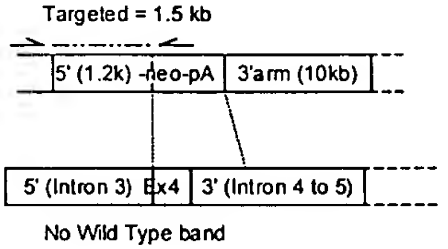

Targeted = 1.5 kb
5' (1.2k) -neo-pA
3'arm (10kb)
5' (Intron 3)
Ex4
3' (Intron 4 to 5)
No Wild Type band

Figure 17